IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF TENNESSEE
NASHVILLE DIVISION

A.J.J.T., an individual minor, by and through his mother and next friend, **KELLY D. WILSON**, and **KELLY D. WILSON**, individually, and **DELVIN D. TAVAREZ**, individually,	)	
Plaintiff,	)	**Case No. 3:15-cv-01073**
v.	)	
UNITED STATES OF AMERICA,	)	
Defendant.	)	

LOCAL RULE 39.01(c)(6)(c) STATEMENT OF EDWARD H. KAROTKIN, M.D.

My name is Edward Karotkin and I am a medical doctor, licensed in the States of Virginia and Maryland. I am a specialist in Pediatrics and Neonatal-Perinatal Medicine, board-certified in both by the American Board of Pediatrics. I have been in the active practice of medicine for more than 40 years.

My education, training, professional experience, and publications are fully set forth in my *curriculum vitae*.

In this matter, I was asked to determine the most probable cause of A.J.J.T.'s problems in the neonatal period and the timing of such cause. Throughout my career, I have personally taken care of children in the NICU similar to A.J.J.T. and have trained and supervised residents and fellows in the diagnosis, care, and treatment of neonates such as A.J.J.T.. My approach in this case is the same as my approach in clinical practice. My methodology is known as differential diagnosis. In reaching a most

probable etiology for a patient's condition, one considers the potential causes and, based on physical exams, testing, laboratory data, and imaging, arrives at the most probable cause. This is the standard method used by all clinicians including neonatologists.

In this matter I was provided with the prenatal and labor and delivery records of Kelly Wilson, the birth and neonatal records of A.J.J.T., and the expert reports of Drs. Michael Hawkins (Ob/GYN), Joseph Bruner (MFM/OB-GYN), Allen Elster (neuroradiology), Garrett Burris (Pediatric Neurology), and Daniel Benjamin (Pediatric infectious Diseases).

The pertinent facts are as follows: A.J.J.T. was delivered by emergency cesarean section at 0801 on January 10, 2005. His mother, Kelly Wilson was 21 years old with a prior cesarean section, Group Beta Strep positive (GBS), and had a history of herpes simplex virus (HSV). According to the obstetrician's report, the cesarean section was called for a non-reassuring fetal heart rate tracing. According to the records, around 0730, while Ms. Wilson was sitting up discussing epidural analgesia, a profound fetal heart rate deceleration to the 60s occurred and did not recover. Dr. Adams, in her operative report, wrote that initially the fetal heart tracings had been reassuring. She also noted at delivery the presence of terminal meconium (fetal stool), clear amniotic fluid, and a grossly normal placenta and umbilical cord. At delivery A.J.J.T. was a normally developed baby, of appropriate size for his gestational age of 39 and 3/7 weeks, weighed 3406 grams with head circumference of 34 cm (70th percentile).

A.J.J.T.'s cord blood was sent to the lab for analysis. The arterial cord blood gas had a pH of 6.762 and base excess of -16.1. The venous blood gas had a pH of 7.157 and

a base excess of -6.4. The arterial cord blood gas reflects a severe fetal metabolic acidosis. This is the result of impaired gas exchange leading to the accumulation of acid in the fetal blood. A cord pH of less than 7.0 and/or a base excess of greater than -12 are associated with neonatal encephalopathy and brain injury. The disparity between the arterial and venous cord gases is noteworthy. The arterial blood is the blood going from the baby to the placenta, the venous blood is the blood coming from the placenta to the baby. The venous blood gas was nearly normal, yet the arterial blood gas was severely acidotic. This disparity indicates that the process producing the acidosis was not of longstanding duration and that the placental function was intact.

A.J.J.T. had no signs of life at delivery. He was flaccid, blue, not breathing, and had no detectable heart rate. His Apgar scores at 1, 5, 10, and 15 minutes of life were 0, 1, 2, and 4, respectively. Apgar scores reflect fetal well-being in the first few minutes of life and the need for resuscitation. The Apgar score assigns points based on the newborn's skin color, pulse rate, reflexes, activity, and respiration. The total points range from 0 to 10. A.J.J.T.'s Apgar scores reflect a newborn with profound depression that required immediate resuscitation. They also reflect a slow response to resuscitation and continued respiratory depression. Dr. Flint, the pediatrician in attendance at delivery, began resuscitation immediately with chest compressions and attempted intubation. Dr. Min, another pediatrician, arrived in the delivery room and assisted with bag-mask positive pressure ventilation and successfully intubated him with a 3.0 endotracheal tube. To address the severe bradycardia (heart rate only 60 beats/minute), A.J.J.T. was given epinephrine and chest compressions were continued until his heart rate improved to the 90s after 10-15 seconds. An emergent

umbilical venous catheter was placed and he was given 10cc normal saline over one minute. He was then transferred to the special care nursery. His heart rate was improved to 110, but his oxygen saturations were still low, at 85%.

A.J.J.T. was placed on a ventilator and started on IV fluids. A blood gas, CBC, and blood cultures were obtained. He was started on antibiotics (Ampicillin and Gentamycin) for possible sepsis. This is a standard practice in the treatment of newborns with birth depression. Sepsis is presumed and treated until it can be excluded. This allows for treatment to begin immediately without waiting as long as several days for blood culture results to become available. A.J.J.T.'s first arterial blood gas found a pH of 7.18 and base excess of -19. This reflects some improvement following resuscitation, yet a persistent acidosis remained. In response, sodium bicarbonate was ordered and given to counter the acid that had persisted in his blood.

Arrangement was then made for A.J.J.T.s transfer to the NICU at Vanderbilt for management and head cooling. At 1000 the nursing staff reported questionable subtle seizure activity. At 1015 the Vanderbilt transport team arrived and assumed care.

Significantly, the blood cultures taken at BACH were negative for bacterial growth at 48 hours and at five days. Ms. Wilson's prophylactic treatment with antibiotics during labor (due to her GBS+ status) was unlikely to cause the cultures to be falsely negative because her antibiotics began less than one hour before delivery. As such, it is not likely that fetal antibiotic levels were sufficient to sterilize the blood sample taken just after delivery.

The CBC including differential count was within normal limits, thus providing no evidence of a severe bacterial infection.

The placenta and umbilical cord were sent to pathology for review. These specimens were evaluated at BACH and sent to the Armed Forces Institute of Pathology. The pathology report from the Armed Forces Institute of Pathology described chorangiosis, necrotizing chorioamnionitis, funisitus, intervillous thrombi, acute and remote retromembranous hemorrhage, meconium staining, and a marginal cord insertion. The report further noted clusters of cocci embedded in the amnion. The samples were tested for the presence of HSV (herpes simplex virus) and CMV (cytomegalovirus) and found to be negative. The placental specimens are significant for the presence of chorioamnionitis/funisitis. It is noteworthy that Ms. Wilson did not exhibit any signs of clinical chorioamnionitis during labor. There was no fever, no uterine tenderness, or foul smelling amniotic fluid reported. There was no fetal tachycardia. The microscopic placental findings raise the possibility of fetal infection, but do not mean, necessarily, that the fetus was infected. One must also consider other data to prove or disprove fetal infection.

A.J.J.T. arrived at Vanderbilt around 1100 and was admitted to the NICU. During transport, he received additional sodium bicarbonate. He remained intubated and on ventilator support. He was started on prophylactic Acyclovir in light of his mother's history of HSV.

A.J.J.T. 's admission physical exam was remarkable for eye deviations, decreased tone, hypoactive bowel sounds, and tremulousness upper extremities and lips. He was started on the 72 hour head cooling protocol for asphyxia. Cerebral spinal fluid cultures and studies were planned along with close observation for seizure-like activity. His

diagnoses at admission included 1) respiratory failure, 2) hypoxia, 3) seizure activity, and 4) metabolic acidosis.

A.J.J.T.'s spinal fluid cultures were negative for bacterial growth. Testing of his CSF for HSV was also negative. In light of his negative blood and CSF cultures and negative HSV test, antibiotics and Acyclovir were stopped on January 13th, day of life three. Thereafter, he remained without signs or symptoms of infection. This is significant in two respects. First, stopping antibiotics shows that the treating neonatologists had not found any evidence to support a diagnosis of bacterial infection. Had they still suspected infection despite the negative cultures, they would have continued antibiotics. Second, A.J.J.T. received less than a full course of antibiotics. Had he truly been septic, three days of antibiotics would have not been sufficient to eliminate the bacteria and he would have developed worsening symptoms.

Electroencephalograms on January 11th and 14th demonstrated encephalopathy. Activity suspicious for seizures was observed on January 11th and he was started on Phenobarbital. A CT of the brain on January 12th was negative for intracranial hemorrhage, infarct, and infection. An MRI taken on March 21, 2006 (14 months later) revealed hyper-intense signal in the periventricular white matter, the posterior putamen bilaterally, and the bilateral thalami. According to the report, the findings likely represent sequela of a perinatal hypoxic ischemic event.

A pediatric neurology consult was obtained on January 13th. The resident's consultation note listed the following impressions 1) birth depression, and 2) possible seizures related to birth depression, and hypoxic-ischemic encephalopathy. The

attending physician concurred, writing, "[o]ur impression is neonatal Hypoxic Ischemic Encephalopathy" with probable development of seizures secondary to this.

A meconium drug screen was ordered and reported negative on January 21. Newborn metabolic and genetic screening was normal.

Hypoxic ischemic encephalopathy (HIE) is the name for a syndrome of disturbed neurologic function due to lack of blood flow and/or oxygen to the brain. It is also referred to as birth asphyxia or perinatal asphyxia. In reaching a diagnosis of hypoxic ischemic encephalopathy, neonatologists look for specific signs such as: evidence of fetal heart rate abnormalities during labor, an abnormal arterial cord blood gas, low Apgar scores, particularly at five and ten minutes, signs of encephalopathy such as seizures, abnormal muscle tone, abnormal EEG, evidence of injury on brain imaging, and often evidence of injury to other organ systems.

In this case, I concur with the treating physicians at Vanderbilt. A.J.J.T.'s clinical findings strongly support a diagnosis of hypoxic ischemic encephalopathy. There was evidence of fetal distress leading to emergency cesarean section. His arterial cord blood gas reflected significant metabolic acidosis. His Apgar scores were low and he required vigorous resuscitation. He exhibited probable seizure activity within 24 hours of delivery and had abnormal neurologic exams and EEGs. Finally, his MRI at 14 months shows a brain injury consistent with hypoxic ischemic injury. Evidence of multi-organ injury included respiratory failure, and some abnormalities in liver function tests and cardiac enzymes in the first two days of life.

Other possible etiologies were also considered. As discussed above, the mother's history of GBS, HSV and the placental pathology findings raise the possibility of

infection. However, the blood cultures, serology, and the baby's continuing improvement despite discontinuation of antibiotics collectively are inconsistent with neonatal infection. Maternal drug abuse was also considered, but the meconium drug screen was negative. A.J.J.T. was full term and his size was appropriate for gestational age. Babies with chronic placental problems tend to be small for gestational age or growth restricted. There was no laboratory evidence of a metabolic disorder, and the routine newborn metabolic screening was normal. Finally, he was not found to have any dysmorphic features that would suggest the possibility of a genetic cause.

Lastly, there is the question of whether the presence of chorioamnionitis and funisitis could have caused A.J.J.T.'s neonatal encephalopathy. The theory would be that the fetal inflammatory response to chorioamnionitis/funisitis would lead to the release of cytokines which could then either directly injure the brain or disrupt the exchange of oxygen and carbon dioxide in utero thereby causing brain injury. While there is some epidemiologic evidence supporting an association in preterm babies, no such association has been proven in term babies. The release of cytokines is a normal physiologic response to stressors. Hypoxia and ischemia are known to trigger the release of cytokines. The theory that cytokine release due to chorioamnionitis/funisitis (without sepsis) leads to neonatal encephalopathy/brain injury in term babies is controversial and not generally accepted. It is my opinion that this theory has no application to this case.

A.J.J.T. remained on the ventilator until January 14th. He was successfully weaned to room air. Activity suspicious for seizures continued and he remained on Phenobarbital. A repeat EEG on January 17th was negative for seizures but consistent

with generalized, non-specific encephalopathy. Phenobarbital was discontinued on January 19th. Over time, he continued to improve in tone, alertness, and feeding. He was discharged from Vanderbilt on February 4, 2005. His diagnoses on discharge were 1) hypoxic-ischemic encephalopathy, and 2) perinatal asphyxia.

In summary, based on my education, training, and professional experience in diagnosing and caring for children like A.J.J.T., it is my opinion that he sustained a significant hypoxic ischemic insult during labor, close to the time of delivery and most probably beginning with the deceleration that prompted emergent cesarean section. This period of hypoxia-ischemia continued through delivery and during resuscitation as reflected by his low Apgar scores, a heart rate in the 60s, absence of spontaneous respirations, and metabolic acidosis that persisted. Other potential causes such as maternal drug use, infection, genetic abnormalities, metabolic disorders, and fetal inflammatory response can be excluded for lack of supporting evidence. The data supporting hypoxia-ischemia in this case is, on the other hand, substantial.

Equally substantial is the evidence that the event occurred close to the time of delivery. First, a baby with acidosis as severe as A.J.J.T.'s would not survive long in utero without delivery. Had this event been remote from delivery, he probably would have been stillborn. This conclusion is also supported by his Apgar scores and need for immediate vigorous resuscitation. Had the event been remote from delivery or of longer duration, he would not have responded to resuscitation. Similarly, the disparity between the arterial and venous cord gases is consistent with an event that was acute, rather than chronic. Also supportive is the MRI at around 14 months of age that reflects injury to the deep grey matter. Injuries to this part of the brain are the result of acute,

severe asphyxia. As such, considering all of the forgoing, it is my opinion that had delivery occurred at any time prior to the fetal heart of 60 that did not recover, the hypoxic ischemic encephalopathy would have not occurred.

Edward H. Karotkin M.D.

Edward H. Karotkin, M.D.

October _____, 2018

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CERTIFICATE OF SERVICE

I hereby certify that on August 6, 2019, a copy of Plaintiffs' Expert Witness Statement of Edward H. Karotkin, M.D. was filed electronically. A copy of said document was served by operation of the Court's electronic filing system on opposing counsel as follows:

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